



[11] Patent Number: 6,007,988

[45] **Date of Patent:** Dec. 28, 1999

- Blause et al. Vectors in cancer therapy: how will they deliver? *Cancer Gene Therapy* vol. 2(4):291-297, Oct./1995.
- Rebar et al: "Zinc Finger Phage: Affinity Selection of Fingers with New DNA-Binding Specificities", *Science*, vol. 263, Feb. 4, 1994, pp. 671-673.
- Jamieson et al: "In Vitro Selection of Zinc with Altered DNA-Binding Specificity", *Biochemistry*, 1994, 33, pp. 5689-5695.
- Thiesen et al: "Determination of DNA binding specificities of mutated zinc finger domains", *FEBS LETTERS*, vol. 283, No. 1, May 1991, pp. 23-26.
- Jacobs: "Determination of the base recognition positions of zinc fingers from sequence analysis", *The EMBO Journal*, vol. 11, No. 12, 1992, pp. 4507-4517.
- Desjarlais et al: "Toward rules relating zinc finger protein sequences and DNA binding site preferences" *Proc.Natl.Acad.Sci.USA*, vol. 89, Aug. 1992, *Biophysics*, pp. 7345-7349.
- Nardelli et al: "Zinc finger-DNA recognition: analysis of base specificity by site -directed mutagenesis", *Nucleic Acids Research*, vol. 20, No. 16, pp. 4137-4144.
- Desjarlais et al: "Use of a zinc-finger consensus sequence framework and specificity rules to design specific DNA binding proteins", *Proc.Natl.Acad.Sci.USA*, vol. 90, Mar. 1993, *Biochemistry*, pp. 2256-2260.

(List continued on next page.)

Primary Examiner—James Ketter
Assistant Examiner—William Sandals
Attorney, Agent, or Firm—Pillsbury, Madison & Sutro LLP;
 Cushman Darby & Cushman IP Group

U.S. PATENT DOCUMENTS

5,498,530	3/1996	Schatz et al.	435/69.1
-----------	--------	---------------	----------

OTHER PUBLICATIONS

Orkin, Report and recommendation of the panel to assess the NIH investment in research on gene therapy, Dec. 7, 1995.
Freisen et al. Phage display of RNA binding zinc fingers from transcription factor IIIA. *J. Biol. Chem.* vol. 272(17):10994-10997, Apr. 25, 1997.

[57] **ABSTRACT**

Disclosed are libraries of DNA sequences encoding zinc finger binding motifs for display on a particle, together with methods of designing zinc finger binding polypeptides for binding to a particular target sequence and, inter alia, use of designed zinc finger polypeptides for various *in vitro* or *in vivo* applications.

41 Claims, 14 Drawing Sheets

[illegible]

OTHER PUBLICATIONS

Choo et al: "Toward a code for the interactions of zinc fingers with DNA: Selection of randomized fingers displayed on phage", *Proc.Natl.Acad.Sci.USA*, vol. 91, Nov. 1994, *Biochemistry*, pp. 11163-11167.

Choo et al: "Selection of DNA binding sites for zinc fingers using rationally randomized DNA reveals coded interactions", *Proc.Natl.Acad.Sci.USA*, vol. 91, Nov. 1994, *Biochemistry*, pp. 11168-11172.

Choo et al: "In Vivo repression by a site-specific DNA-binding protein designed against an oncogenic sequence", *Nature*, vol. 372, Dec. 15, 1994, pp. 642-645.

Wu et al: "Binding zinc fingers by selection: Toward a therapeutic application", *Proc.Natl.Acad.Sci.USA*, vol. 92, Jan. 1995, *Biochemistry*, pp. 344-348.

Klug et al: "Zinc Fingers", *The FASEB Journal*, May 1995, vol. 9, No. 8, pp. 597-604.

Choo et al: "Designing DNA-binding proteins on the surface of filamentous phage", *Current Opinion in Biotechnology*, 1995, 6: pp. 431-436.

11163-11167